UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF NORTH CAROLINA

AMY BRYANT, MD, *Plaintiff*, v. JOSHUA H. STEIN *et al.*, *Defendants*, and PHILIP E. BERGER, *et al.*, *Intervenor-Defendants.*	No. 1:23-cv-77

DEFENDANT ATTORNEY GENERAL JOSHUA H. STEIN'S MEMORANDUM OF LAW IN OPPOSITION TO INTERVENOR-DEFENDANTS' AMENDED MOTION TO DISMISS

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INTRODUCTION

For more than two decades, the Food and Drug Administration has approved and regulated mifepristone, a drug used for the medical termination of early pregnancy. Based on extensive evidence, the agency has determined that mifepristone is safe and that serious complications are extremely rare.

The FDA regulates mifepristone pursuant to express statutory authority, which empowers the agency to weigh the benefits of the drug against its risks and to impose conditions on its administration. 21 U.S.C. § 355-1(a)(1). These conditions — also known as a Risk Evaluation and Mitigation Strategy, or REMS — reflect the agency's expert judgment on the best way to balance drug safety, efficacy, and access. *Id.* § 355-1(f).

Since approving mifepristone in 2000, the FDA has regularly modified the drug's REMS based on the evidence that has been compiled across two decades of use. More specifically, the FDA has rescinded certain conditions that, in the agency's expert scientific judgment, are no longer necessary to ensure the drug's safety.

North Carolina law nonetheless imposes some of the very same restrictions on mifepristone that the FDA has implemented and then subsequently withdrawn. Under settled preemption principles that the Supreme Court has applied for decades, the

Supremacy Clause does not permit States to frustrate the considered judgment of a federal agency in that manner.

To be sure, States ordinarily have wide latitude to enact laws protecting the health and safety of their citizens. Indeed, state law traditionally "offers an additional, and important, layer of consumer protection that complements FDA regulation." *Wyeth v. Levine*, 555 U.S. 555, 579 (2009). But when, as here, state law imposes the same rules that a federal agency has deliberately rescinded, state law must yield. As the Supreme Court has made clear, when a "federal statutory scheme amply empowers the FDA . . . to achieve a somewhat delicate balance of statutory objectives," state laws that "skew[ ]" this balance are preempted. *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 348 (2001); *see also Geier v. American Honda Motor Co.*, 529 U.S. 861, 878-89 (2000).

Legislative Intervenors' contrary arguments are unpersuasive. They claim that the FDA regulations in this context set a "floor" and that States may therefore enact additional restrictions. But the state laws that Plaintiff challenges here do not merely supplement federal standards; instead, they directly interfere with a balance that Congress empowered the FDA to strike because they impose regulations that the agency adopted and later rescinded.

Legislative Intervenors also argue that the FDA's regulations cannot preempt state law because REMS are not formal agency action. But REMS are imbued with the force of law — they are restrictions implemented by the FDA following formal administrative procedures authorized by Congress, and they carry weighty monetary and injunctive penalties for violations. REMS therefore have preemptive force.

Finally, Legislative Intervenors argue that the FDA REMS cannot preempt state law because mifepristone is used for abortions, and abortion is a "major question." But nothing in *Dobbs v. Jackson Women's Health Org.*, 142 S. Ct. 2228 (2022), or any other case, curtails the FDA's statutory authority to balance the risks and benefits of certain drugs and impose conditions for their safe use. Failure to apply ordinary preemption principles to this conflict between state and federal law merely because it involves abortion would nullify decades of Supreme Court preemption precedents.

For these reasons, this Court should hold that the mifepristone REMS preempts the challenged North Carolina laws to the extent that they impose restrictions on mifepristone that the FDA previously included, but ultimately removed.

FACTUAL BACKGROUND

I. STATUTORY AND REGULATORY FRAMEWORK.

States have "great latitude under their police powers to legislate as to the protection of the lives, limbs, health, comfort, and quiet of all persons." *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 475 (1996); *see also Gonzales v. Oregon*, 546 U.S. 243, 270 (2006) (the "structure and limitations of federalism" generally leave regulating the practice of medicine to the states). This latitude ordinarily extends to regulating how healthcare professionals administer drugs. *Whalen v. Roe*, 429 U.S. 589, 603 n.30 (1977).

While regulating the practice of medicine is generally reserved for the States, since 1938, Congress has charged the FDA with overseeing the safety, marketing, and distribution of food, drugs, and cosmetics. 21 U.S.C. § 301 *et seq.* Specifically as to drugs, the FDA must "promote the public health" by ensuring that "drugs are safe and effective." *Id.* § 393(b)(1), (2). One way the FDA fulfills this mandate is through its role in approving drugs for sale. Under the Food, Drug, and Cosmetic Act, a drug manufacturer cannot introduce a drug into interstate commerce unless the FDA grants it marketing approval. *Id.* § 355(b). To obtain FDA approval, the manufacturer must prove that the drug is safe and effective "for

use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof." *Id.* § 355(d); *see also* 21 C.F.R. § 314.125(b).

In 2007, Congress gave the FDA additional authority to issue REMS requirements for certain drugs. REMS requirements are, in essence, specific conditions that ensure that a drug's benefits outweigh its risks. *Id.* § 355-1(a)(1). In issuing REMS, the FDA must consider specific statutory factors, including the size of the population likely to use the drug, the drug's expected benefit, the expected or actual duration of treatment, and the seriousness of known or potential adverse events caused by the drug. *Id.* § 355-1(a)(1). Congress gave the FDA full authority to determine which drugs are subject to a REMS and what requirements a REMS should impose.

At the same time, Congress expressly cabined the FDA's authority over REMS plans by requiring the agency to "assur[e] access and minimiz[e] burden." § 355-1(f)(2). Specifically, the FDA must ensure that REMS requirements: (1) are "commensurate with the specific serious risk" of the drug, (2) are not "unduly burdensome on patient access to the drug," and (3) "to the extent practicable," "minimize the burden on the health care delivery system." *Id.* §§ 355-1(f)(2)(A), (C), (D).

To achieve this delicate balance, Congress authorized the

FDA to use the REMS program to regulate the administration of drugs by healthcare providers, a function ordinarily reserved for the States. For example, as part of a REMS strategy, the FDA may require that healthcare providers who prescribe a drug have particular training or experience; that pharmacies, practitioners, or healthcare settings that dispense a drug be specially certified; that a drug be dispensed to patients with documentation of its safe-use conditions; that patients be subject to certain monitoring while using a drug; or that patients using a drug be enrolled in a registry. *Id.* §§ 355-1(f)(3)(A), (B), (C), (D), (E), (F).

Recognizing that drug safety requires continually revisiting all available evidence, Congress directed the FDA to review REMS requirements periodically. *Id.* § 355-1(f)(5)(B). As part of the review process, the FDA can add, remove, or modify REMS requirements when doing so would help "ensure the benefits of the drug outweigh [its] risks" or would "minimize the burden on the health care delivery system of complying" with the REMS. *Id.* § 355-1(g)(4)(B)(ii).

REMS are not merely guidance documents. Before adopting or modifying a REMS, the FDA must follow detailed and formal administrative procedures. These procedures include, for example, reviewing the proposed REMS or modification within 180

days, *id.* § 355-1(h)(2)(A)(i); and reviewing any modifications due to labeling changes or other minor modifications within 60 days, *id.* §§ 355-1(h)(2)(A)(ii), (iii). If there is a dispute about a REMS, the FDA must resolve it, in consultation with the Drug Safety Oversight Board, through a formal review process that is open for public comment. *Id.* § 355-1(h)(4). After a REMS is put in place, moreover, the FDA conducts inspections to evaluate compliance. Failure to comply with REMS requirements may result in a range of different enforcement actions, including product seizures, injunctions, or civil penalties.[1]

To date, the FDA has issued REMS for just 61 drugs.[2]

II. THE FDA'S APPROVAL AND REMS CONCERNING MIFEPRISTONE.

In 2000, the FDA approved the drug mifepristone for use in terminating early pregnancies, subject to certain conditions. (First Am. Compl.~~, Ex. C~~ (Doc. 82~~-3~~)). Today, mifepristone is also widely prescribed for the management and treatment of other reproductive medical issues, including miscarriages, uterine

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[1] REMS Compliance Program, U.S. Food and Drug Administration, *available at* https://www.fda.gov/drugs/risk-evaluation-and-mitigation-strategies-rems/rems-compliance-program (last accessed Apr. 4, 2023). Courts "routinely take judicial notice of information contained on state and federal government websites." *United States v. Garcia*, 855 F.3d 615, 621 (4th Cir. 2017).

[2] Approved Risk Evaluation and Mitigation Strategies (REMS), U.S. Food and Drug Administration, *available at* https://www.accessdata.fda.gov/scripts/cder/rems/ (last accessed Apr. 19, 2023).

fibroids, and endometriosis.[3]

Since the FDA first approved mifepristone in 2000, it has modified the drug's REMS requirements on multiple occasions, most recently earlier this year.

A. FDA's Initial Approval in 2000.

On September 28, 2000, after reviewing more than 90 submissions regarding safety and efficacy, the FDA approved Mifeprex (the trade name for mifepristone) for use in terminating pregnancies. (First Am. Compl.~~, Ex. C~~ (Doc. ~~1-3~~82)). As part of the approval, the FDA attached several conditions for the drug's use, among them:[4]

- Mifeprex could be prescribed only by a physician who had the ability to assess the duration of pregnancy, to diagnose ectopic pregnancies, and to provide or arrange for surgical intervention if necessary. (First Am. Compl.~~, Ex. C~~ (Doc. ~~1-3~~82)).

- Mifeprex could be provided only "by or under the supervision of a physician." (*Id.*)

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[3] Mifepristone: Questions and Answers with Rollins Researchers, Emory University Rollins School of Public Health (Apr. 13, 2023), *available at* https://sph.emory.edu/news/news-release/2023/04/mifepristone-questions-answers.html (last accessed Apr. 19, 2023).

[4] The FDA imposed these restrictions under 21 C.F.R. § 314 Subpart H. Subpart H restrictions are one of the precursors to REMS. When Congress enacted the REMS framework in 2007, it deemed drugs with existing Subpart H restrictions to have approved REMS imposing the same restrictions. Pub. L. No. 110-85, Tit. IX, § 909(b) (21 U.S.C. § 331 note). Since 2007, the REMS framework has dictated the appropriate use of mifepristone.

B. FDA's Subsequent Implementation of a REMS in 2011.

In 2007, when Congress enacted the REMS framework, it required manufacturers of drugs that had already been approved with additional conditions under Subpart H (like mifepristone) to submit a proposed REMS for approval. Food and Drug Administration Amendments Act § 909(b). In 2011, the FDA approved the proposed REMS for mifepristone. The 2011 REMS mirrored the restrictions that had been adopted as part of the Subpart H regulations. (First Am. Compl., Exs. H, I (Docs. 821-8, 821-9.))

C. FDA's Modification of the REMS in 2016.

In 2016, after further study, the FDA "assessed the current REMS program to determine whether each Mifeprex REMS element remains necessary to ensure that the drug's benefits outweigh the risks." (First Am. Compl., Ex. J (Doc. 821-10).) The FDA conducted a comprehensive review of the drug's safety and efficacy based on "20 years of experience with [mifepristone], guidelines from professional organizations here and abroad, and clinical trials that have been published in peer-reviewed medical literature."[5] Nothing in this review prompted the FDA to alter its finding that mifepristone is safe and effective. But the FDA did

[5] Medical Review, Application Number: 020687Orig1s020, Center for Drug Evaluation and Research, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/nda/2016/020687Orig1s020MedR.pdf (last accessed Apr. 19, 2023).

conclude that the REMS for mifepristone needed to be "modified to continue to ensure that the benefits of Mifeprex outweigh its risks and to minimize the burden on the healthcare delivery system of complying with the REMS." (First Am. Compl., Ex. J (Doc. 821-10)).

The FDA modified the REMS in two respects relevant here. First, the FDA expanded the practitioners who may prescribe Mifeprex from "physicians" to a broader class of "healthcare provider[s]," which included nurse practitioners, certified midwives, and physician assistants. (First Am. Compl., Ex. L (Doc. 821-12)). Second, while the FDA retained the requirement that the drug be *dispensed* to the patient in the healthcare provider's office, the FDA eliminated the requirement that the patient *take* the drug there. (*Compare* First Am. Compl., Ex. N (Doc. 821-14). *with* First Am. Compl., Ex. H (Doc. 821-8)).

D. FDA's Further Modification of the REMS in 2023.

In 2021, the FDA again undertook a full review of the mifepristone REMS. (First Am. Compl., Ex. Q (Doc. 821-17)).[6] As part of this review, the FDA conducted extensive

[6] Separately, in April 2021, amid the COVID-19 pandemic, the FDA announced that it would exercise its discretion and decline to enforce the requirement that mifepristone be dispensed only in certain healthcare settings. Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation, U.S. Food & Drug Admin., *available at* https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-mifepristone-medical-termination-pregnancy-through-ten-weeks-gestation (last accessed Apr. 27, 2023).

analysis of published safety data, including longitudinal data related to medication abortion, systemic reviews, and meta-analyses. (*Id.*) The FDA again found nothing to alter its conclusion from 2000 that mifepristone is safe and effective.

The FDA did, however, again decide to make certain modifications to the REMS to minimize the burden on the healthcare delivery system, healthcare providers, and patients. (First Am. Compl., Ex. R (Doc. 821-18); (First Am. Compl., Ex. T (Doc. 821-20).) In particular, the FDA eliminated the requirement that mifepristone be dispensed in a healthcare provider's office. Specifically, the FDA found that this in-person dispensing requirement was "no longer necessary to ensure the benefits of mifepristone outweigh the risks of serious complications," and that eliminating this requirement would help "minimize the burden on the healthcare delivery system of complying with the REMS." (First Am. Compl., Ex. R (Doc. 821-18)). The FDA thus modified the REMS to allow certified pharmacies to begin dispensing mifepristone, starting in 2023. (*Id.*)

III. NORTH CAROLINA'S LAWS REGULATING MIFEPRISTONE USE.

North Carolina, like many States, has laws related to medical and surgical abortion. Plaintiff specifically challenges how those state laws affect access to mifepristone.

As the chart below demonstrates, many of the state laws at issue here restrict mifepristone access in ways that the FDA originally adopted. But critically, the FDA has since rescinded those restrictions, consistent with Congress's directive to balance the risks of mifepristone against the burden that restrictions impose on healthcare delivery systems and patients.

North Carolina Law/Regulation	**Subpart H/ 2011 REMS**	**2016 REMS**	**2023 REMS**
Mifepristone must be dispensed only by a "qualified physician." N.C. Gen. Stat. § 14-45.1(a).	Similar restriction.	Expanded access by allowing mifepristone to be dispensed by a qualified non-physician healthcare provider.	Mifepristone may be dispensed by a qualified non-physician healthcare provider.
A "qualified physician" must be present when mifepristone is administered to the patient. N.C. Gen. Stat. § 90-21.82(1)(a).	Similar restriction.	Eliminated the restriction.	No similar restriction.

Mifepristone can be dispensed only in a hospital or clinic that is specially certified by the North Carolina Department of Health and Human Services (and that conforms to a variety of building codes and facility-requirements). *Id.* §§ 14-45.1(a), 14-45.1(a1), 10A N.C. Admin. Code §§ 14E.0101(2), .0104, .0105, .0203, .0204, .0205, .0206.	Similar restriction.	Similar restriction.	Eliminated the restriction.

ARGUMENT

I. THE CHALLENGED STATE LAWS ARE PREEMPTED BECAUSE THEY UNLAWFULLY INTERFERE WITH THE CAREFUL BALANCE THE FDA STRUCK IN PROVIDING PATIENT ACCESS TO MIFEPRISTONE.

In designing the REMS for mifepristone, the FDA carried out its statutory obligation to carefully balance the risks of the drug against the need to minimize burdens on patient access and the health care delivery system. 21 U.S.C. § 355-1(f)(2). As the FDA has continued to calibrate the optimal balance over the last 23 years, it has modified and removed certain restrictions from the REMS. Several of the state laws that Plaintiff challenges impose the same restrictions that the FDA adopted and then rescinded, thereby frustrating the FDA's framework. As a

result, these state-law conditions must yield to the FDA's considered judgment.

A. Longstanding Preemption Principles Forbid States From Enforcing Laws and Regulations That Frustrate a Federal Framework.

"[B]ecause the States are independent sovereigns in our federal system," courts have "long presumed" that state laws are not preempted by federal statutes. *Medtronic, Inc.*, 518 U.S. at 485. This presumption against preemption is especially strong in "field[s] which the States have traditionally occupied." *Id.* (quoting *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230 (1947)). Public health and safety is one such area, given that it has "primarily, and historically, [been] a matter of local concern." *Hillsborough Cnty. v. Automated Medical Labs. Inc.*, 471 U.S. 707, 719 (1985); *see also Metropolitan Life Ins. Co. v. Massachusetts*, 471 U.S. 724, 756 (1985) ("States traditionally have had great latitude under their police powers to legislate as to the protection of the lives, limbs, health, comfort, and quiet of all persons." (internal quotations omitted)). The Supreme Court has consistently refused to infer "an intent to pre-empt" "state and local regulation related to matters of health and safety" and has instead found that such laws "can normally coexist with federal regulations." *Hillsborough Cnty.*, 471 U.S. at 718; *see also Medtronic, Inc.*, 518 U.S. at 485.

Although the presumption against preemption plays a critical role in protecting state sovereignty, it can be overcome in rare cases. For instance, if a state law "actually conflicts" with federal law, the state law must yield. *Ray v. Atlantic Richfield Co.*, 435 U.S. 218, 230 (1947). Such a conflict can occur when state law "prevent[s] or frustrate[s] the accomplishment of a federal objective," or when it "make[s] it impossible for private parties to comply with both state and federal law." *Geier*, 529 U.S. at 873; *see also Hillman v. Maretta*, 569 U.S. 483, 490 (2013). In both instances, the conflicting state law is "nullified" by the Supremacy Clause. *Geier*, 529 U.S. at 873.

"To determine whether a state law conflicts with Congress' purposes and objectives," courts must "first ascertain the nature of the federal interest." *Hillman*, 569 U.S. at 491. The Supreme Court has long recognized a strong federal interest in preserving a comprehensive federal regulatory scheme. *See, e.g.*, *Geier v. American Honda Motor Co.*, 529 U.S. 861, 874-75 (2000) (finding a federal interest in a particular regulatory scheme regarding automobile safety). This federal interest is particularly significant when Congress authorizes an expert federal agency to comprehensively regulate complex or technical subject matter by balancing "difficult (and often competing)

objectives." *Buckman Co.*, 531 U.S. at 349-50 (recognizing a strong federal interest in preserving the FDA's ability to police fraud as part of the difficult task of regulating the marketing and distribution of medical devices).[7]

Where a state law imposes restrictions that a federal agency has considered and rejected in enacting a comprehensive regulatory scheme, the Supreme Court has repeatedly held that that state law is preempted. Take, for instance, the Supreme Court's decision in *Geier*. In that case, the plaintiffs invoked state tort law to sue a car manufacturer for failing to install passenger-side airbags. 529 U.S. at 876. But the car manufacturer's airbags decision had not occurred in a vacuum. Under the federal motor-vehicle-safety regulatory scheme in place at the time, the Department of Transportation had deliberately balanced public safety, public acceptance, technological advances, and cost. *Id.* at 878-79. And in so

[7] *See also Geier*, 529 U.S. at 883 (recognizing a strong federal interest in maintaining a comprehensive scheme where Congress "delegated to [the Department of Transportation] the authority to implement [a safety-standards] statute" because the agency is "likely to have a thorough understanding of its own regulation and its objectives and is uniquely qualified to comprehend the likely impact of state requirements") (internal quotations omitted); *Int'l Paper Co. v. Ouellette*, 479 U.S. 481, 494-95 (1987) (recognizing a strong federal interest in EPA's authority to set water quality standards because the agency had to weigh the existence of available technology, competing public and industrial uses, the impact of the discharges on the waterway, and the types of effluents).

doing, DOT had specifically *rejected* requiring mandatory airbags in every car, in favor of a more varied mix of passive-restraint systems. *Id.* Allowing state tort lawsuits for failure to install airbags would therefore have frustrated federal interests by imposing a requirement that DOT had specifically considered and rejected. *Id.* at 880-81. As a result, the Supreme Court held that the state tort lawsuit was preempted. *Id.* at 882.

United States v. Arizona is of a piece. That case involved an Arizona statute that imposed criminal penalties on immigrants who sought, or engaged in, unauthorized employment. 567 U.S. 387, 404-05 (2012). In finding this state law preempted, the Supreme Court stressed that Congress had "made a deliberate choice not to impose criminal penalties on aliens who seek, or engage in, unauthorized employment." *Id.* at 405. The Arizona law therefore stood as an obstacle to the federal regulatory system, which provided for civil penalties alone. *Id.* at 406.

Here, the case for preemption is even stronger. As shown below, the FDA did not merely consider and reject regulations of the kind that state law imposes. Rather, the FDA affirmatively implemented restrictions on mifepristone and then deliberately rescinded them pursuant to its statutory mandate to balance drug safety, efficacy, and access. Under Supreme Court precedent,

States may not undermine an agency's judgment by imposing through state law the same regulations that the agency has rescinded.

B. North Carolina's Laws Regulating the Use of Mifepristone Frustrate the FDA's Regulatory Regime and Are Therefore Preempted.

Several of the laws and regulations that Plaintiff challenges violate these well-settled preemption principles. Over the last 23 years, the FDA has regularly modified the restrictions that apply to the prescription and administration of mifepristone, including by rescinding certain restrictions after evidence established that they were no longer necessary. North Carolina law nevertheless attempts to impose some of these same now-rescinded federal restrictions. The Supremacy Clause does not permit States to frustrate the considered judgment of a federal agency in that manner. As a result, the challenged laws must yield.

For nearly a century, the FDA has been responsible for ensuring that drugs are "safe and effective" before they are introduced into interstate commerce. 21 U.S.C. §§ 393(b)(1), (2). One mechanism that the FDA uses to ensure safe use is the development of a REMS, which seeks to "ensure that the benefits of [a] drug outweigh the risks." *Id.* § 355-1(a)(1).

Since 2000, when the FDA first approved mifepristone, that

drug has been subject to a REMS (or the Subpart H equivalent). But the restrictions composing the REMS have changed over time. Initially, a physician alone could prescribe mifepristone, mifepristone could be dispensed only by a physician, and patients had to take the drug in the presence of a physician. (First Am. Compl.~~, Ex. C~~ (Doc. 82~~1-3~~)). In the two decades since, the FDA has materially altered all of these regulations, based on "20 years of experience . . . , guidelines from professional organizations here and abroad, and clinical trials that have been published in peer-reviewed medical literature."[8]

Now, a range of "health care providers" (*e.g.*, nurse practitioners, certified midwives, and physician assistants) can prescribe mifepristone; the drug can be dispensed by certified pharmacies (not just physicians at certain health care facilities); and a physician need not be present when a patient takes the drug. (First Am. Compl., Ex. L (Doc. 82~~1~~-12); First Am. Compl., Ex. R (Doc. 82~~1~~-18)).

The North Carolina laws that Plaintiff challenges impose some of the same restrictions that the FDA has eliminated from the mifepristone REMS. First, state law requires that mifepristone be dispensed by "a qualified physician." N.C. Gen.

[8] Medical Review, Application Number: 020687Orig1s020, Center for Drug Evaluation and Research, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/nda/2016/020687Orig1s020MedR.pdf (last accessed Apr. 19, 2023).

Stat § 14-45.1(a). Second, state law requires that a physician be present when mifepristone is administered to the patient. *Id.* § 90-21.82(1)(a). Third, state law requires that mifepristone be dispensed only in a hospital or clinic that is specially certified by the North Carolina Department of Health and Human Services (and conforms to a variety of building codes and facility-requirements). N.C. Gen. Stat. §§ 14-45.1(a), 14-45.1(a1), 10A N.C. Admin. Code §§ 14E.0101(2), .0104, .0105, .0203, .0204, .0205, .0206.

These three sets of challenged laws directly contradict the reasoned balance that the FDA – at Congress's direction - has reached. Specifically, the laws impose restrictions that the FDA included in the mifepristone REMS, but ultimately rescinded, based on the agency's considered judgment that they unduly burdened patient access and the healthcare delivery system, without providing effective benefits.[9]

This regime runs afoul of the Supremacy Clause. Congress authorizes the FDA to place restrictions on a drug's prescription and administration, and that authority is used by the FDA to achieve the delicate (and statutorily mandated)

[9] In May 2023, the North Carolina General Assembly enacted Session Law 2023-14 over the Governor's veto. On August 7, the plaintiff amended her complaint to challenge several provisions contained in this new law as well. Doc. 82. But, in accordance with this Court's August 7 order instructing the Attorney General to file his opposition to the Legislative Intervenors' motion to dismiss making changes only to conform the citations in the amended complaint (Doc. 81), the Attorney General does not discuss those additional challenges here.

balance of maintaining safety while ensuring access. The challenged state laws disrupt the balance that the FDA has struck by imposing conditions on mifepristone that the agency originally put in place but later explicitly rejected. The correct lesson to draw from the agency's decision is that the FDA decided to rescind these conditions because they "would be inappropriate." *Arizona*, 567 U.S. at 406. Thus, the state laws must yield. *See Buckman Co.*, 531 U.S. at 348 (where a "federal statutory scheme amply empowers the FDA to punish and deter fraud against the [FDA]," state tort law cannot "skew[]" the "delicate balance" that the agency puts in place); *see also Geier*, 529 U.S. at 878-82.

II. LEGISLATIVE INTERVENORS' ARGUMENTS TO THE CONTRARY FAIL.

Legislative Intervenors try to overcome these well-settled principles with a range of arguments. Each fails.

First, Legislative Intervenors argue that the FDA can set the "floor" regarding the safe use of drugs, but that "states are free to regulate above the floor established by FDA regulation." (LD Br. at 15-16, 27-28). Ordinarily, Legislative Intervenors may well be right. State laws that regulate drugs more stringently than federal regulations are typically complementary, not contradictory. *See, e.g.*, *Wyeth*, 555 U.S. at 579 (respecting FDA authority to preempt state law, but holding that the FDA did not take overt action to do so in that case).

Here, however, North Carolina's laws restricting the use of mifepristone effectively override the FDA's considered judgment, because they impose restrictions that the FDA deliberately rescinded. *See supra* Part I.B. Preemption doctrine cannot countenance a conflict of that kind. *See supra* Part I.A; *see also, e.g.*, *Geier*, 529 U.S. at 878-82; *Arizona*, 567 U.S. at 404.; *Buckman Co.*, 531 U.S. at 348.

Next, Legislative Intervenors argue that REMS plans lack the force of law and, thus, that the regulations cannot preempt state law. (LD Br. at 20). Legislative Intervenors are wrong. Agency action "carries force of law when, first, Congress has 'delegated authority to the agency generally to make rules' and, second, the 'agency [action] was promulgated in the exercise of that authority." *Sierra Club v. U.S. Dep't of the Interior*, 899 F.3d 260, 286 (4th Cir. 2018). Courts will also consider the extent to which Congress "provides for a relatively formal administrative procedure" as the mechanism for agency action. *Welch v. Chao*, 536 F.3d 269, 276 n.2 (4th Cir. 2008). The mifepristone REMS plainly satisfies all of these requirements. Congress specifically authorized the FDA to issue REMS through a formal administrative procedure, including formal dispute resolution, agency review, and public comment. 21 U.S.C. §§ 355-1(a), (h)(2), (4). In addition, failure to comply with REMS requirements may result in enforcement action, such as product

seizure, injunction, or civil money penalties.[109] As a result, REMS are the kind of "agency regulation with the force of law" that can preempt conflicting state law. *Wyeth*, 555 U.S. at 576.

Finally, Legislative Intervenors attempt to undermine Plaintiff's arguments using the "major questions doctrine." (LD Br. at 15-20.) As they see things, Congress did not give the FDA authority to regulate medication abortion "in all fifty states." (LD Br. at 13.) Hence, they contend, the FDA cannot preempt the challenged laws without running afoul of the "major questions doctrine." (LD Br. at 13.)

Legislative Intervenors' argument falls flat. Courts will apply the major questions doctrine when a federal agency "assert[s] highly consequential power" that arguably goes "beyond what Congress could reasonably be understood to have granted." *West Virginia v. EPA*, 142 S. Ct. 2587, 2609 (2022). Nothing of the sort has happened here. The agency action at the heart of this case is the development of a REMS for mifepristone, and Congress's grant of authority to the FDA to develop REMS plans is crystal clear. 21 U.S.C. § 355-1. Legislative Intervenors do not dispute that Congress has given

[109] REMS Compliance Program, U.S. Food and Drug Administration, *available at* https://www.fda.gov/drugs/risk-evaluation-and-mitigation-strategies-rems/rems-compliance-program (last accessed Apr. 4, 2023).

the FDA authority to regulate drugs and to impose conditions meant to ensure their safe administration. Nor do they dispute that mifepristone is a drug that falls within the scope of the FDA's regulatory authority.[10] *See* LD Brief at 2 (conceding that "the FDCA . . . require[s] the FDA to implement safety measures over the use of dangerous drugs, including the chemical-abortion drug Mifeprex").

Recall again the history behind the mifepristone REMS: The FDA first passed restrictions on the use of mifepristone in 2000, pursuant to its authority under Subpart H. Seven years later, Congress itself determined that any drugs that had in effect "elements to assure safe use" — including those with Subpart H restrictions — would be deemed to have a REMS. *See* FDAAA § 909(b)(1), 121 Stat. at 950-51. At the time, this group contained sixteen drugs, mifepristone among them.[11] This history simply cannot be reconciled with an argument that Congress might

[10] A separate set of plaintiffs have brought a challenge to the FDA's approval and REMS of mifepristone in 2000, 2016, and 2023 in a separate federal action, *Alliance for Hippocratic Medicine v. United States Food and Drug Admin.*, No. 22-cv-2223-Z, 2023 U.S. Dist. LEXIS 61474 (N.D. Tex. 2023). But that challenge relies on the procedures required under the Administrative Procedure Act — the plaintiffs have not argued that the FDA lacks authority to regulate mifepristone or that the mifepristone REMS violates the major questions doctrine.

[11] Identification of Drug and Biological Products Deemed to Have Risk Evaluation and Mitigation Strategies for Purposes of the Food and Drug Administration Amendments Act of 2007, 73 Fed. Reg. 16,314, 16,315 (Mar. 27, 2008).

not have intended the FDA to have authority to determine the conditions for safe use of mifepristone.

Instead, Legislative Intervenors argue that Congress has not granted the FDA sweeping authority "to set national abortion policy." (LD Brief at 17.) This argument is a red herring. By developing a REMS for mifepristone, the FDA does not purport to set abortion policy nationwide. States across the country can — and have — enacted vastly divergent laws regarding abortion, and Plaintiff does not argue that all these state laws must yield. Rather, Plaintiff argues that Congress has granted the FDA the authority to weigh the risks and benefits of certain drugs and impose conditions for their safe use. On this score, Plaintiff is clearly correct.

Plaintiff's position, moreover, is entirely consistent with the Supreme Court's recent decision in *Dobbs v. Jackson Women's Health Org.*, 142 S. Ct. 2228 (2022). (LD Brief at 17) *Dobbs* held that the federal constitution does not protect a woman's right to an abortion. It did not nullify the Supremacy Clause – or the longstanding preemption principles that arise from that provision - in the realm of reproductive rights. In passing abortion laws, then, States may not contradict the considered judgment of Congress or the FDA.

CONCLUSION

For the foregoing reasons, the North Carolina laws that restrict the use of mifepristone in a manner that the FDA adopted, but later rejected, are preempted. Laws of that kind pose an obstacle to the purposes and objectives of Congress and frustrate its decision to vest the FDA with the authority to balance drug safety, efficacy, and access by developing REMS for certain drugs.

Dated: ~~April 28~~August 16~~21~~, 2023 Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

I hereby certify that the foregoing brief complies with Local Rule 7.3(d) because, excluding the parts of the brief exempted by Rule 7.3(d) (cover page, caption, signature lines, and certificates of counsel), this brief contains fewer than 6,250 words. This brief also complies with Local Rule 7.1(a).

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